Quarterly Newsletter | Issue 4 October - December2020



MedNews If you want to know more...

Where in the world are Esco Medical devices installed

The year 2020 is about to end and we all have seen a general "slowdown" in various economic activities brought about by the pandemic. Nonetheless, we, at Esco Medical, opted to recognize and embrace these sudden changes as we remain steadfast in providing our customers across the globe their IVF needs.

More installations were made in various parts of the world, and we are beyond grateful for this continuous support.







Esco Medical US Team advances further into the Animal Fertility Market

The US Team has recently installed a 4-foot, MAW with MIRI chambers and will soon install a MIRI benchtop incubator in the B Equal Genetics Equine Fertility Lab at the prestigious Sterling Ranch, Texas. This is the first breeding-specific Equine Fertility Lab, and third laboratory in the equine field, to invest in Esco Medical equipment.

Sterling Ranch is set on 120 acres of North Texas prairie in the heart of Horse Country USA. The ranch features a stateof-the art mare and foal barn where foaling out can be electronically monitored from the staff living quarters inside the building. In the breeding area, there is a large modern laboratory and semen shipping center as well as facility for frozen semen storage.

We, at Esco Medical, continue to make headway in this new and exciting segment in the world of fertility!



Texas, USA

Clinic name: B Equal Genetics Equine Fertility Lab Installed: 2020 Equipment: Esco Multi-Zone ART Workstation 4feet with MIRI® Chambers

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Batam Island, Indonesia

Clinic name: Awal Bros. IVF Clinic Installed: October 26, 2020 Equipment: MIRI® Multiroom Incubator, Esco Multi-Zone ART Workstation and CelCulture® CO₂ Incubator

Jakarta, Indonesia

Clinic name: Morula IVF Installed: December 2015 Equipment: MIRI[®] TL Incubators, MIRI[®] Multiroom Incubator, Esco Multi-Zone ART Workstations, and CelCulture[®] CO₂ Incubator









Georgia

Clinic name: Germai Georgian Reproductive Center GGRC Installed: 2020 Equipment: MIRI[®] Multiroom Incubator



Italy

Clinic name: Progetto Salute Sas Di Guarneri Installed: December 10, 2020 Equipment: MIRI® TL Incubator, 6 Chambers



Belgium

Clinic name: Cliniques Universitaires de Bruxelles – Hopital Erasme Installed: December 9, 2020 Equipment: MIRI[®] TL 6 and 12 Chambers



Berlin, Germany

Clinic name: Fertility Center Berlin Installed: December 10, 2020 Equipment: MIRI[®] Multiroom Incubator



Pakistan

Clinic name: Australian Concept Infertility Medical Center (ACIMC) - Karachi Installed: October 3, 2020 Equipment: MIRI[®] TL Incubator, 6 Chambers





Sudan

Clinic name: Royal Care Hospital Installed: 2020 Equipment: MIRI[®] Multiroom Incubator







UAE

Clinic name: HealthPlus UAE Installed: March 2019 Equipment: MIRI[®] Multiroom Incubato

ART Techniques

Couples confronted with infertility and related problems should be made aware that there are alternatives to treat such condition. A set of techniques called assisted reproductive technology (ART) help couples get pregnant. Each of which brings about varying degrees of success for different instances. Here is a summary of 4 popular ART techniques.

$$\mathsf{GIFT} \bigcirc + 222 = 222 \bigcirc \rightarrow \bigcirc \bigcirc \bigcirc$$

Gamete intra-fallopian transfer or GIFT: A procedure wherein the doctor extracts eggs and sperm, combine them, and then transplant into the fallopian tubes. The reinsertion happens via laparoscopy (an operation performed in the abdomen or the pelvis using small incisions with the use of a camera) so long as the tubes are healthy. The aim is to let the egg and sperm fertilize naturally.



Zygote Intra-fallopian Transfer or ZIFT: Almost similar with GIFT, this transfer technique refers to a procedure in which a woman's oocytes are taken from her ovaries, undergoes fertilization in the laboratory (in vitro), and eventually inserted into her fallopian tubes instead of the uterus. Both techniques happen within 24 hours for maximum effect and would also require laparoscopy.

Dairy Products: Fertility Boosters?



We often hear people talking about which food to eat during pregnancy and even after giving birth. But, did you know that there are certain foods that could boost one's fertility?

Some notable food includes lean-protein options like turkey, chicken or beef that are considered to be good iron sources. It is believed that women who have iron-rich diet are more inclined to be fertile than ladies who are deficient of it. Others highly recommend the increased intake of whole grains, fruits like berries, and seafood like oysters and salmon – all believed to boost one's ability to conceive.

But from among these fertility boosters, dairy products like whole milk are highlighted to be essential. Dairy, in general, is a must for women who want to conceive since it is rich in calcium, hence, vital for bone and reproductive health.



In vitro fertilization or IVF: The most popular ART procedure wherein both GIFT and ZIFT are considered IVF techniques. Done in a laboratory setting, the sperm cells are placed together with an unfertilized egg in a dish to bring about fertilization, and eventually, the development of an embryo. The embryo is ultimately transferred into the woman's uterus. IVF is regarded as the gold standard of ART techniques.



Intracytoplasmic sperm injection or ICSI: A fertility procedure that has changed the game for male factor infertility. Traditional IVF requires that the extracted sperm and egg interact and potentially fertilize without any help. However, with ICSI, the clinician injects the sperm cell directly into the egg cell. This manipulation technique that requires the use of a microscope to aid during the injection of that single sperm into the egg cells before the fertilized eggs are transferred into the woman's body.

Infertility remains to be a serious concern from among childless couples. Fortunately, today's advances in technology has presented struggling couples an array of options.

Several studies have shown results that support the significance of dairy products (especially whole milk) from among women undergoing infertility treatment.

The result of a study published in 2016 entitled "Dairy intake in relation to in vitro fertilization outcomes among women from a fertility clinic" shows that there was a positive association between total dairy food consumption and live birth among women \geq 35 years of age. During the study, the participants' diet was evaluated prior to Assisted Reproductive Technology (ART) treatment.

On the other hand, a Harvard prospective study on dairy foods intake and anovulatory infertility was published in 2007 wherein it was concluded that a high intake of low-fat dairy foods may increase the risk of anovulatory infertility while the intake of highfat dairy foods may cut this risk.

In 2017, two preconception cohort studies about "dairy intake and fecundability" were conducted from among women planning for pregnancy. Results show that there was no clear relationship between low- or high-fat dairy intake and the probability of conceiving a clinically recognized pregnancy in either cohort. However, there was little evidence of association between dietary intake of vitamin D, and minerals like calcium, potassium, magnesium, and even phosphorus, and fecundability.

While it is true that no specific food or fertility diet can miraculously boost one's chances of conceiving, a healthy and balanced diet definitely helps maintain over-all reproductive health, in both men and women. Eat healthy!

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Organizational Chart of Esco Medical: Europe, MENA and USA

Europe

	Position
Denmark	
Jesper Lindhardsen	Sales Director
Mehrdad Makky	BDM
Morten Kristensen	Service & installation Specialist
Ricky Lindgaard Nielsen	R&D Manager
Germany	
Sanjay Bhjowani	BDM
Lithuania	
Nerijus Baliunas	Factory Production Head
Vaida Zubraite-Puike	Quality Assurance Manager
Stasys Polimaitis	Customer Service Manager
Evaldas Peciunas	Service Manager
Monika Chreptaviciute	Service & Installation Coordinator
Ricardas Naujokas	TL Software Engineer
Domantas Armonavicius	Products Specialist



MENA

Mehrdad Makky	
Alaa Mohammed Bieruti	
Mary Castillo	

USA

Richard Seiler
William Zembricki
Andrew Spinelli
Julienne Viuya
Maureen Snyder
Jason Ma (Part Time)

Position
Sales
Sales
Service Technician
Service Engineer
Service Engineer/ Service Scheduling
Service Engineer

Position Sales Engineer Service Engineer

Operations



A Quick Look at today's IVF Industry

Assisted reproductive technologies (ART) are quickly progressing, allowing more people to overcome their infertility. Through the years, a remarkable increase in the accessibility and availability of different fertility treatments across the world has been noted. In the United States alone, infertility is believed to affect approximately 10% of the reproductive age populace. Consequently, the use of ART is growing (not only in the United States), but across the globe, as this technology holds to improve pregnancy rates, hence more couples seek and rely on medical support as a means of dealing with infertility. With such growing concerns, it is not surprising that the in vitro fertilization (IVF) industry has seen tremendous growth in its market in the past years.

1. What comprises the IVF Market

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- 2. IVF Products
- 3. IVF Technologies
- 4. IVF End-Users
- 5. IVF Geography
- 6. Esco Medical and IVF Manufacturers

What comprises the IVF Market

The IVF industry seems to be a small niche. However, scrutiny will make one realize that it is a significant market. It is divided into the following segments:

- 1. Product: (Instruments, accessories, consumables/ disposables, and reagent & media)
- 2. Technology (Fresh Embryo IVF, Frozen Embryo IVF, and Donor Egg IVF)
- 3. End Users (Fertility Clinics, Hospitals, and Other End Users)
- 4. Geography (North America, Europe, Asia-Pacific, Middle-East and Africa, and South America)

The increasing growth of the IVF devices and consumables industry is foreseen to be determined by various factors. Such influences include the following: delay in pregnancies among women, rise in worldwide infertility rates, advancement in IVF technology and the increase in the success rate of ART, increase in reproductive cell donations, and even the increase in disposable revenue. Moreover, the flourishing of fertility tourism, especially in evolving markets, growth in the number of fertility clinics and laboratories, and even the increase in same-sex marriages are expected to bring about profitable growth opportunities to the IVF industry per se.

IVF Products

According to the product, the IVF market is further grouped into instruments, accessories & disposables, and reagent & media.

1. The instrument segment: This includes sperm separation

systems, cryosystem (a system for producing, maintaining, or handling low temperatures), incubators (Esco Medical's MIRI line of products are notable examples), ovum aspiration pump, cabinet, or workstations (eg. Esco Medical's MAW), micromanipulator, imaging system, and others.

- 2. Accessories and disposables: These are products that are designed to be disposed instead of being refilled or repaired (disposables like Esco Medical's CultureCoin[®], a culture dish specifically used for the MIRI TL incubator), and a finished device that is used to provide support, or amplify the function of one or more parent device (accessory).
- **3. Reagent & media:** A sub-segment of IVF products (complex solutions) that are used to support cell growth. Such products include embryo culture media, cryopreservation media, sperm and egg cell processing media.

It is believed that this segment serves as the major revenue contributor. Furthermore, it is expected that IVF products will lead the market in the coming years since these products are perceived to play important role in all IVF procedures/ techniques like embryo handling, sperm and egg retrieval.

IVF Technology

When (IVF) was first established, "fresh transfers" were the only kind of transfer offered since cryopreservation or embryo freezing was not yet fully developed and was mainly for future use. But with the various advances in ART, freezing techniques, use of culture media, and development of other reproductive technologies, the use of both fresh and frozen embryo transfers has become more readily available.

According to technology, the IVF market is divided into the following:

- 1. Fresh Embryo IVF: This transfer usually occurs 5 days after the patient's egg cells are retrieved. Afterward, the eggs are fertilized with sperm in the laboratory, to which the resultant embryo is grown and observed.
- 2. Frozen Embryo IVF: This transfer usually happens 6-8 weeks after the embryo is frozen. Once the patient is prepared for transfer, medications that imitate the natural menstrual cycle are given. The transfer date then is coordinated with the cycle to improve the implantation procedure.
- **3.** Donor Egg IVF: This involves the use of another woman's egg cells. The eggs are usually taken from a qualified donor (one who is young, healthy, and fertile). It then undergoes fertilization and implantation into the recipient's uterus.

Currently, the fresh embryo IVF segment is regarded as the major

revenue contributor. Based on forecasts made by experts, this form of transfer will continue to show control since it is established to bring about a higher success rate, cost-effectiveness, and greater safety for the patient.

IVF End-Users

The IVF devices and consumables market is also divided into the kind of end-user. This would include fertility clinics, hospitals, IVF surgical centers, and clinical research institutions. Fertility clinics are the most popular and probably the most frequently visited setting by patients. These are medical clinics that support couples, and even individuals, who want to become parents but are unable to achieve the goal of having a child. They are often manned by skilled and qualified professionals that include reproductive endocrinologists, embryologists, nurses, sonographers, and other IVF clinicians.

Such clinics offer various fertility programs and are equipped with essential IVF devices in their laboratories.

IVF Geography

While there are an increasing number of IVF facilities, manufacturers, and patients across the world, the following countries in specific regions are noteworthy to mention since studies about IVF and ART, in general, have been conducted.

For North America, the U.S.A has played a vital role together with Canada, and Mexico). Europe, being the home of the ESHRE - European Society of Human Reproduction and Embryology (an important organization across the continent), has been actively promoting ART/ IVF guidelines, and an increase in the IVF market is significantly observed in countries like Germany, France, the United Kingdom, Italy, and Spain. The Asia-Pacific region is slowly becoming an important hub for the IVF industry with China, Japan, Australia, India, and Southeast Asian country like Singapore paving the way for more opportunities.

IVF Manufacturers

The success of the IVF industry has been remarkable in the past years because of the IVF devices and consumables manufacturers and distributors. The innovations created by these companies have made a huge impact on the success of pregnancy rates across the world. Prominent key players in the IVF industry include Fujifilm Holdings Corporation, Vitrolife, Cook Medical Inc., The Cooper Companies, Inc. (CooperSurgical, Inc.), Thermo Fisher Scientific, Inc., and Esco Lifesciences. (Esco Medical)

Esco Medical is the IVF (medical technology) business unit of Esco, a renowned Singapore-based life science company with a diversified portfolio and sales in over 100 countries.

Esco Medical delivers innovative technological solutions for fertility clinics and laboratories. It is regarded as one of the leading manufacturers of high-quality equipment such as longterm embryo incubators, Assisted Reproductive Technology (ART) workstations, anti-vibration tables, and time-lapse incubators. Esco Medical is continuously developing advanced technologies to meet the increasing demand of the IVF industry.



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IVF Trivia: How long can human embryos stay frozen?

October 26, 2020

A healthy baby girl (Molly Everette Gibson) was born from an embryo that had been frozen for 27 years. This is believed to be the record for the longest time a human embryo has stayed frozen prior being born.

1992

The year the embryo was frozen and stored in a cryogenic freezer in the Midwest region of the United States.

2012

The embryo was placed into a liquid nitrogen shipping vessel and sent to an embryo adoption facility.

February 2020

The embryo was implanted into the uterus of Tina Gibson (who was only 1 year old when the embryo was frozen).

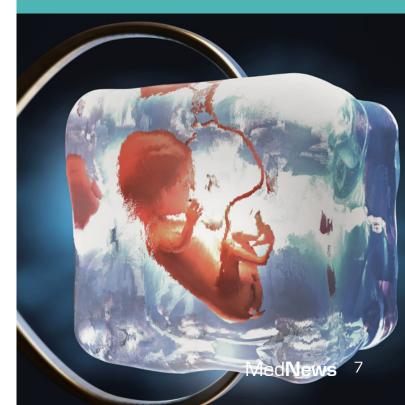
Interesting to note that Molly's case broke the record set by her own biological older sister, Emma Gibson, who was also conceived through IVF. Emma's embryo was frozen for 24 years before Tina Gibson gave birth to her.

Question is:

How long can human embryos stay frozen?

Barry Behr of Stanford University Medical Center says that human embryos stay frozen "indefinitely". By subjecting the embryo to cryopreservation, it will bring about the ceasing of all biological activities. Moreover, Dr. Mary Ellen Pavone of Northwestern Medicine in Illinois, gave a supporting statement that indeed embryos can "be pretty much stored indefinitely" with modern freezing techniques.

Interesting and amazing IVF facts! (Information taken from www.livescience.com)





Genome Editing on Human Embryos Are we ready for it?

Throughout the years, several technological advancements in the field of IVF have emerged and helped increase the success rates of IVF clinics across the world. With the scientific community continuously growing, innovations need to be kept in check with proper ethical restrictions and regulations in place. Such breakthroughs should pass certain levels of clearances and evaluations from the scientific boards before moving to the next stages of clinical trials especially before starting with human trials (human embryos in this matter).

One innovation, in particular, is the use of CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats – associated protein 9) for genome editing purposes to eliminate or correct diseasecausing mutations present in the chromosomes carrying them. The discovery of the clinical use of CRISPR was lauded in the scientific community because it opened doors to countless possibilities that can greatly help in treating human genetic diseases. Since then, many types of research were done to use this technology on animals and even adult humans who have terminal illnesses and therefore cannot pass on the mutations/corrections brought about by the editing of CRISPR gene therapy. Last November 2018 during the Second International Summit on Human Genome Editing, a report of the first genome editing on human embryos using the CRISPR-Cas9 has surfaced and gathered the attention and scrutiny of the global scientific community.

He Jiankui, together with his team from the Southern University of Science and Technology in Shenzen, has claimed that they have successfully performed genome editing on human embryos (specifically on the gene for CCR5, which is the cellular receptor for HIV) and have also resulted in the birth of the twins (CRISPR babies) with the edited genome. Information about the whereabouts or the current status of the twins was not disclosed by He Jinakui. Although this was indeed a great leap forward to treat human genetic diseases, some say that this was too soon and too many steps ahead of the supposed progress of CRISPR technology trials. Unlike on advanced age adult humans, gene editing on the embryo level can be passed on to future generations and therefore can alter the human gene pool in general. Another study earlier this year was conducted by Columbia University Irving Medical Center to demonstrate that besides the former risk mentioned, the use of the CRISPR-Cas9 gene editing can also produce another detrimental effect to human embryos.

Dr. Dieter Egli and his team have conducted a study to observe the repair outcomes by the CRISPR-Cas9 gene editing on the EYS (eyes shut homolog) locus which carries the frameshift mutation causing hereditary blindness. They have concluded that Cas9-induced double-strand break (DSB) to correct the mutation at the EYS locus resulted in half of the breaks remaining unrepaired for on-target cleavages and they also observed that the Cas9 off-target cleavages may result in total chromosome losses. Dr. Egli even mentioned that "If our results had been known two years ago, I doubt that anyone would have gone ahead with an attempt to use CRISPR to edit a gene in a human embryo in the clinic".

Some scientists have called out for the halt of use of CRISPR technology but some have asserted that the CRISPR babies incident may have made a huge impact on the ethical side of using such technology, but future studies should instead follow the proper and correct way to conduct clinical trials especially in the earlier stage of human development (human embryos) because this will greatly affect the gene pool of humans.



Manufacturer: Esco Medical Technologies, Ltd.

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